

Claims

*July 31*

1. A method for delivery of dendritic cells to a secondary lymphoid tissue of a subject, comprising  
providing isolated genetically modified dendritic cells which express on the cell  
surface a selectin polypeptide comprising an endothelial selectin ligand binding portion of a selectin selected from the group consisting of L-selectin, E-selectin and P-selectin, and  
administering the isolated genetically modified dendritic cells to the subject.
2. The method of claim 1, wherein the secondary lymphoid tissue is ~~peripheral lymph~~  
nodes.
3. The method of claim 1, wherein the secondary lymphoid tissue is appendix.
4. The method of claim 1, wherein the secondary lymphoid tissue is tonsil.

*July 31 2002*

5. A method for delivery of dendritic cells to a non-lymphoid tissue of a subject where selectin ligands are expressed on endothelial cells, comprising  
providing isolated genetically modified dendritic cells which express on the cell surface a selectin polypeptide comprising an endothelial selectin ligand binding portion of a selectin selected from the group consisting of L-selectin, E-selectin and P-selectin, and  
administering the isolated genetically modified dendritic cells to the subject.
6. The method of claim 1 or 5, wherein the selectin polypeptide consists of a selectin selected from the group consisting of L-selectin, E-selectin and P-selectin.
7. The method of claim 1 or 5, wherein the step of providing isolated dendritic cells comprises isolating dendritic cells from the subject and transfecting the isolated dendritic cells with a nucleic acid molecule which encodes the selectin polypeptide.
8. The method of claim 7, wherein the nucleic acid molecule is an ~~expression~~ vector.
9. The method of claim 8, wherein the expression vector is selected from the group

consisting of retroviruses, lentiviruses, adenoviruses and lambda bacteriophages.

10. The method of claim 9, wherein the expression vector is a retrovirus.

5 11. The method of claim 7, wherein the step of providing isolated dendritic cells further comprises culturing the isolated transfected dendritic cells to expand the isolated transfected dendritic cells.

Suba

10 12. The method of claim 1 or 5, wherein the step of providing isolated dendritic cells further comprises treating the isolated transfected dendritic cells with isolated activated platelets or membrane microparticles thereof which contain P selectin.

15 13. The method of claim 1 or 5, wherein the isolated dendritic cells are administered intravenously.

14. A method for delivery of dendritic cells to a secondary lymphoid tissue of a subject, comprising

providing isolated dendritic cells,

treating the isolated dendritic cells with isolated activated platelets or membrane microparticles thereof which contain P selectin to form platelet modified dendritic cells, and administering the isolated platelet modified dendritic cells to the subject.

15. The method of claim 14, wherein the secondary lymphoid tissue is peripheral lymph nodes.

25 16. The method of claim 14, wherein the secondary lymphoid tissue is appendix.

17. The method of claim 14, wherein the secondary lymphoid tissue is tonsil.

30 18. A method for delivery of dendritic cells to a non-lymphoid tissue of a subject where selectin ligands are expressed on endothelial cells, comprising providing isolated dendritic cells,

treating the isolated dendritic cells with isolated activated platelets or membrane microparticles thereof which contain P selectin to form platelet modified dendritic cells, and administering the isolated platelet modified dendritic cells to the subject.

*sub 23*

5 19. The method of claim 14 or 18, wherein the step of providing isolated dendritic cells further comprises culturing the isolated dendritic cells to expand the isolated dendritic cells.

10 20. The method of claim 14 or 18, wherein the isolated platelet modified dendritic cells are administered intravenously.

15 21. A method for delivery of dendritic cells to a secondary lymphoid tissue of a subject, comprising

providing isolated dendritic cells,

15 providing isolated activated platelets or membrane microparticles thereof which contain P selectin,

administering the isolated dendritic cells and the isolated activated platelets or membrane microparticles thereof to the subject, wherein the isolated activated platelets or membrane microparticles thereof are administered prior to or concurrently with the isolated dendritic cells.

20 22. The method of claim 21, wherein the secondary lymphoid tissue is peripheral lymph nodes.

25 23. The method of claim 21, wherein the secondary lymphoid tissue is appendix.

24. The method of claim 21, wherein the secondary lymphoid tissue is tonsil.

25 25. A method for delivery of dendritic cells to a non-lymphoid tissue of a subject where selectin ligands are expressed on endothelial cells, comprising

30 providing isolated dendritic cells,

providing isolated activated platelets or membrane microparticles thereof which contain P selectin,

administering the isolated dendritic cells and the isolated activated platelets or membrane microparticles thereof to the subject, wherein the isolated activated platelets or membrane microparticles thereof are administered prior to or concurrently with the isolated dendritic cells.

5

26. The method of claim 21 or 25, wherein the step of providing ~~isolated dendritic cells~~ further comprises culturing the ~~isolated dendritic cells~~ to expand the isolated dendritic cells.

27. The method of claim 21 or 25, wherein the isolated dendritic cells and the isolate 10 activated platelets are administered intravenously.

28. A composition comprising isolated genetically modified dendritic cells which express on the cell surface a selectin polypeptide comprising an endothelial selectin ligand binding portion of a selectin selected from the group consisting of L-selectin, E-selectin and P-selectin.

29. The composition of claim 28, wherein the selectin polypeptide consists of a selectin selected from the group consisting of L-selectin, E-selectin and P-selectin.

30. The composition of claim 28, wherein the amount of the ~~selectin polypeptide~~ expressed on the cell surface is greater than the naturally occurring amount of the selectin [expressed on the cell surface *in vitro*] and is sufficient to target the genetically modified ~~dendritic cells~~ to peripheral lymph nodes.

25 31. The composition of claim 28, wherein the isolated dendritic cells are transfected with a nucleic acid molecule which encodes the selectin polypeptide.

32. The composition of claim 31, wherein the nucleic acid molecule is an expression vector.

30 33. The composition of claim 32, wherein the expression vector is selected from the group consisting of retroviruses, lentiviruses, adenoviruses and lambda bacteriophages.

34. The composition of claim 33, wherein the expression vector is a retrovirus.

35. The composition of claim 28, further comprising isolated activated platelets or membrane microparticles thereof which contain P selectin.

36. A composition comprising isolated dendritic cells and isolated activated platelets or membrane microparticles thereof which contain P selectin.

37. A vaccine composition comprising the composition of any of claims 28-36 and an antigen.

38. The vaccine composition of claim 37, wherein the antigen is a peptide.

39. The vaccine composition of claim 37, wherein the isolated dendritic cells are loaded with the antigen *ex vivo*.

40. The vaccine composition of claim 37, whereip the isolated dendritic cells are transfected with a nucleic acid molecule which encodes the antigen.

41. The vaccine composition of claim 40, wherein the nucleic acid molecule encodes at least two antigens.

42. The vaccine composition of claim 37, wherein the antigen is selected from the group consisting of MAGE, MART, LAGE, NY-ESO-1, tyrosinase, PRAME, prostate specific antigen (PSA), BCR-ABL, T cell receptor from T cell tumors, immunoglobulins from B cell tumors, RAS and carcinoembryonic antigen (CEA).

43. The vaccine composition of claim 37, further comprising an adjuvant.

44. The vaccine composition of claim 43, wherein the adjuvant is a nucleic acid molecule encoding a polypeptide adjuvant transfected into the isolated dendritic cells

ஒப்பு பாடங்கள்

45. The vaccine composition of claim 43 or 44, wherein the adjuvant is selected from the group consisting of IL-12, GM-CSF, CD40, CD80 and CD86.

46. The vaccine composition of claim 43 or 44, wherein the adjuvant orients an immune response to lymphocyte subsets, wherein the adjuvant is selected from the group consisting of IL-4 and interferon- $\gamma$ .

47. The vaccine composition of claim 43 or 44, wherein the adjuvant is selected from the group consisting of IL-10 and TGF- $\beta$ .

48. A method for stimulating an immune response to an antigen in a subject comprising administering to the subject the vaccine composition of any of claims 37-46.

49. A method for inhibiting an immune response to an antigen in a subject comprising administering to the subject the vaccine composition of claim 47.

50. A method for testing the immunogenicity of an antigen, comprising providing a subject, administering to the subject the vaccine composition of any of claims 37-46, wherein the immunogenicity of the antigen is not known, and determining the immune response of the subject to the antigen.